ABUSE-PROOFED DOSAGE FORM

This application is a continuation of U.S. patent application Ser. No. 15/587,501, filed May 5, 2017, which is a continuation of U.S. patent application Ser. No. 15/245,424, filed Aug. 24, 2016; now U.S. Pat. No. 9,675,610; which is a continuation of U.S. patent application Ser. No. 14/527,911, filed Oct. 30, 2014, abandoned, which is a continuation of U.S. patent application Ser. No. 14/069,439, filed Nov. 1, 2013, abandoned, which is a continuation of U.S. patent application Ser. No. 13/803,789, filed Mar. 14, 2013, abandoned, which is a continuation of U.S. patent application Ser. No. 13/572,926, filed Aug. 13, 2012, abandoned, which is a continuation of Ser. No. 13/365,742, filed Feb. 3, 2012, abandoned, which is a continuation of U.S. patent application Ser. No. 12/822,719, filed Jun. 24, 2010, abandoned, which is a divisional of U.S. patent application Ser. No. 11/007,887, filed Dec. 9, 2004, now U.S. Pat. No. 7,776,314, which is a continuation-in-part of International Patent Application No. PCT/EP2003/006314, filed Jun. 16, 2003, which claims foreign priority benefit under 35 U.S.C. § 119 of the German Patent Applications Nos. 102 50 083.5, filed Oct. 25, 2002, and 102 27 077.5, filed Jun. 17, 2002, the entire disclosures of which patent applications are incorporated herein by reference.

The present invention relates to a solid dosage form with reduced parenteral abuse containing, in addition to one or more active ingredients with potential for abuse, at least one viscosity-increasing agent in quantities such that, on extraction with the assistance of a necessary minimum quantity of aqueous liquid, a gel is formed which can still preferably pass through a needle, which gel, however, remains visually distinguishable even after being introduced into a further quantity of an aqueous liquid.

Many pharmaceutical active ingredients, in addition to having excellent activity in their appropriate application, also have potential for abuse, i.e. they can be used by an abuser to bring about effects other than those intended. Opiates, for example, which are highly active in combating severe to very severe pain, are frequently used by abusers to induce a state of narcosis or euphoria.

Dosage forms which contain active ingredients with potential for abuse, even when taken orally in an abusively large quantity, do not usually give rise to the result desired by the abuser, namely a rapid rush or "kick", because blood levels of the active ingredients increase only slowly. In order nevertheless to achieve the desired effects and enable abuse, the corresponding dosage forms are comminuted, for example ground, by the abuser and the active ingredient is extracted from the powder obtained by comminution of the dosage form with the assistance of a preferably aqueous liquid, preferably the minimum quantity necessary, and the resultant solution, optionally after filtration through cotton wool or cellulose wadding, is administered parenterally, in particular intravenously. Due to this parenteral administration, only the smallest possible quantities of an aqueous liquid are used for extraction, in particular so as to obtain the smallest possible injection volume with active ingredient which results in the desired rapid rush or "kick". In this manner, parenteral administration, in comparison with oral administration, tends to give rise to an accelerated rise in levels of the active ingredient providing the abuser with the desired result.

In order to prevent this form of abuse, it has been proposed in U.S. Pat. No. 4,070,494 to prevent the extraction of an active ingredient from a dosage form by the addition of a swellable agent. On addition of water, this agent swells and ensures that only a small quantity of active ingredient containing liquid is obtained which can be administered parenterally by the abuser. The majority of this dosage form which has swollen is cannot be administered.

A corresponding approach to the prevention of parenteral abuse also underlies the multilayer tablet disclosed in WO 95/20947 which contains the active ingredient with potential for abuse and one or more gel formers each in different layers.

According to this prior art teaching, the viscosity-increasing agents are added in quantities such that the corresponding gel cannot be administered with the assistance of conventional hypodermic needles.

The object of the present invention was to provide a dosage form with at least reduced potential for abuse for active ingredients having with such potential, which dosage form prevents any preferably still possible parenteral, in particular intravenous, abuse of the active ingredients.

This object has been achieved by the provision of the solid dosage form according to the invention with at least reduced potential for parenteral abuse, which dosage form, in addition to one or more active ingredients with potential for abuse, comprises at least one viscosity-increasing agent in a quantity such that a gel which may preferably still pass through a needle is formed in an extract obtained from the dosage form with the assistance of a necessary minimum quantity of an aqueous liquid, which gel remains visually distinguishable when introduced into a further quantity of an aqueous liquid.

For the purposes of the present invention, visually distinguishable means that the active ingredient-containing gel formed by extraction from the dosage form with the assistance of a necessary minimum quantity of aqueous liquid, when introduced with a hypodermic needle with a diameter of 0.9 mm into a further quantity of aqueous liquid at 37° C., remains substantially insoluble and cohesive and cannot straightforwardly be dispersed in such a manner that it can safely be administered parenterally, in particular intravenously. The material preferably remains visually distinguishable for at least one minute, preferably for at least 10 min.

The increase in viscosity of the gel with the assistance of the selected viscosity-increasing agent means that, although this has been rendered more difficult, the gel may still be passed through a needle or injected. It also means that when the resultant extract or gel is introduced at 37° C. into a further quantity of aqueous liquid, for example also by injection into blood, a largely cohesive thread is initially obtained which, while it may be broken up into smaller fragments by mechanical action, it cannot be dispersed or even dissolved in such a manner that it may safely be administered parenterally, in particular intravenously.

Intravenous administration of such an extract would most probably result in obstruction of blood vessels, associated with serious embolism or even death of the abuser.

For the purposes of the present invention, an extract or gel obtained from the dosage form according to the invention with the assistance of a necessary minimum quantity of an aqueous liquid, preferably water, is deemed to be passable through a needle if the gel formed in this manner can still be drawn up and injected back out of a hypodermic needle with a diameter of 2 mm, preferably of 1.5 mm, particularly preferably of 0.6 mm. Pharmaceutical active ingredients with potential for abuse are known to the person skilled in the art, as are the quantities thereof to be used and processes for the production thereof, and may be present in the dosage form according to the invention as such, in the form of